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1: Matsumoto A, Motozaki K, Seki T, Sasaki R, Kawabe T. Related Articles, Links

Expression of human brain carboxypeptidase B, a possible cleaving enzyme for beta-amyloid precursor protein, in peripheral fluids.
Neurosci Res. 2001 Mar;39(3):313-7.
PMID: 11248371 [PubMed - indexed for MEDLINE]

2: Matsumoto A, Itoh K, Matsumoto R. Related Articles, Links

A novel carboxypeptidase B that processes native beta-amyloid precursor protein is present in human hippocampus.
Eur J Neurosci. 2000 Jan;12(1):227-38.
PMID: 10651877 [PubMed - indexed for MEDLINE]

May 2 2005 17:45:08

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L2	1	brain near4(carboxypeptidase adj B)	USPAT	OR	OFF	2005/05/17 20:24
L3	51	human near4(carboxypeptidase adj B)	USPAT	OR	OFF	2005/05/17 20:24
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=> s brain (4A) (carboxypeptidase (w) B)
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=> s l1 and APP
L2            10 L1 AND APP

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AN 2002405327 EMBASE
TI **Brain**-specific **carboxypeptidase B**: Selective down-regulation in ependymal cell by irradiation and altered β-amyloid processing.
AU Kawabe T.; Sasaki R.; Nishimura H.; Soejima T.; Matsuyama S.; Sugimura K.; Matsumoto A.
CS T. Kawabe, Division of Radiology, Kobe Univ. Grad. School of Medicine, Kusunoki-cho, Kobe 650-0017, Japan
SO Neuroscience Research Communications, (2002) Vol. 31, No. 2, pp. 75-84.
Refs: 23
ISSN: 0893-6609 CODEN: NRCOEE
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
014 Radiology
029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 20021121
Last Updated on STN: 20021121
AB Human **brain carboxypeptidase B** (HBCPB) is a **brain** protease expressed in a group of neuronal perikarya and ependymal cells, and cleaves β-amyloid precursor protein (**APP**) in vitro, generating β-amyloid (Aβ)-bearing C-terminal fragment of **APP**. To explore its physiological function, response to external stress, such as ionizing radiation, and expression in mouse brain were studied. Mouse head was irradiated at 10 Gy, then brains were excised before or after 1h until 9 d of irradiation. They were analyzed using TUNEL assay and anti C14-module antibody which detects epitopes unique to HBCPB, and western analysis. The mouse HBCPB-homologue cleaved mouse brain **APP** in vitro. Morphological study indicated its identical distribution to HBCPB. During 2 h after irradiation, the

HBCPB-homologue expression in edendymal cells, but not in neurons, decreases transiently, and recovers within 4 h. Concomitantly, processing of **APP** is altered, increasing generation of the C-terminal 12 kDa fragment. Since **APP** participates in cellular response to tolerance in CNS, this finding suggests that radiation-induced APP processing and differential response in its expression between ependymal cells and neurons are associated with important physiological function in CNS.

L3 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 2
AN 2001339416 MEDLINE
DN PubMed ID: 11248371
TI Expression of human **brain carboxypeptidase B**, a possible cleaving enzyme for beta-amyloid precursor protein, in peripheral fluids.
AU Matsumoto A; Motozaki K; Seki T; Sasaki R; Kawabe T
CS Department of Radiation Biophysics and Genetics, Kobe University School of Medicine, Kusunoki-cho chuo-ki 7-5-1, Kobe650-0017, Japan.. amat@med.kobe-u.ac.jp
SO Neuroscience research, (2001 Mar) 39 (3) 313-7.
Journal code: 8500749. ISSN: 0168-0102.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200106
ED Entered STN: 20010618
Last Updated on STN: 20010618
Entered Medline: 20010614
AB Human **brain carboxypeptidase B** (HBCPB) is a novel **brain** protease that processes native brain beta-amyloid precursor protein (**APP**) in vitro. Immunoblot analysis of human serum and cerebrospinal fluid (CSF) using anti C14-module antibody, which recognizes the C-terminal peptide unique to HBCPB, detected the 30 and 40 kDa immunoreactive bands. Analysis of HBCPB prepared from both serum and CSF demonstrated proteolytic activities for brain **APP**. Protease inhibitor spectrum analysis also supports that these bands correspond to the mature form and and prepro form of HBCPB, respectively. As is the case in brain parenchyma, the prepro-form is dominant in CSF. In serum,

however, the majority of HBCPB exists in the mature form, possibly due to an abundant trypsin-like proteolytic activity in serum. HBCPB expressed in serum and CSF, therefore, may have a significance as a peripheral marker of the brain protease, which participates in **APP** processing in human brain.

L3 ANSWER 3 OF 4 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 3
AN 2001:533671 BIOSIS
DN PREV200100533671
TI Distribution of a human **brain carboxypeptidase B** capable of cleaving beta-amyloid precursor protein (**APP**) in normal and Alzheimer's diseased brain.
AU Itoh, Kyoko [Reprint author]; Matsumoto, Akira
CS Department of Neurosciences, School of Medicine, Case Western Reserve University, 2109 Adelbert Rd, Rm 658, Cleveland, OH, 44106-4975, USA
SO Acta Histochemica et Cytochemica, (2001) Vol. 34, No. 4, pp. 275-283.
print.
CODEN: ACHCBO. ISSN: 0044-5991.
DT Article
LA English
ED Entered STN: 14 Nov 2001
Last Updated on STN: 23 Feb 2002
AB The processing of beta-amyloid precursor protein (**APP**) is considered critical for understanding the pathogenesis of Alzheimer's disease (AD). To elucidate the significance of **APP** processing enzyme, we studied immunohistochemically the distribution of **APP**-processing protease (human carboxypeptidase B: HBCPB) in the normal control brains and AD brains, using anti-C14 antibody which recognizes C-terminal 14 amino acids of HBCPB. In the control brains, intense and diffuse C14-immunoreactivity was observed in the cytoplasm of pyramidal neurons of the hippocampus. Moderate immunoreactivity was found in the cortical and subcortical neurons. In AD brains, C14-immunoreactivity was markedly decreased in the brain regions examined except for the brain stem and cerebellum. However, HBCPB was shown to be colocalized with beta-amyloid protein (Abeta) in neuritic plaques. In addition, neuritic

plaques included C14-immunoreactive microglia/macrophages. Our present
studies indicate that the expression of a novel **APP**-processing
protease is impaired in AD brains and may suggest the possible role of
HBCPB in the pathogenesis of AD.

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:790617 CAPLUS
DN 133:346507
TI Human **brain carboxypeptidase B**, cDNA, and
use in drug screening and disease diagnosis
IN Matsumoto, Akira
PA Japan
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066717	A1	20001109	WO 2000-JP2878	20000501
EP 1179588	A1	20020213	EP 2000-922936	20000501

PI WO 2000066717 A1 20001109 WO 2000-JP2878 20000501
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
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CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1179588 A1 20020213 EP 2000-922936 20000501
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO
PRAI JP 1999-125169 A 19990430
WO 2000-JP2878 W 20000501

AB A novel human **brain carboxypeptidase B**
(CPB), its cDNA, recombinant expression, antibody, and use in screening of
ligands, activators, and inhibitors, are disclosed. Use as beta amyloid

(Aβ) production regulator, and therapeutic agent for diseases related to Aβ accumulation in brain such as senile dementia, Alzheimer's disease, Down's syndrome, hereditary cerebral hemorrhage, head contusion, is claimed. Diagnosis of and diagnostic reagent kits for those diseases are also claimed. A novel carboxypeptidase B with amyloid precursor protein (**APP**) cleaving activity was identified from human hippocampus and its cDNA was cloned by screening human hippocampus cDNA library. Northern blot anal. for tissue distribution, Western blot anal. with polyclonal antibodies, immunohistochem. studies, and homol. searches, were carried out. Enzyme activity studies showed that Aβ1-40 and Aβ1-42 were substrates.

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